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EXAMINER	
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ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,480	SILVER ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,13-17 and 19-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,13-17 and 19-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1 May 2008 has been entered.

Claims 6, 13-17 and 19-25 were considered in the Final Office Action mailed 5 February 2008. Claims 6, 19 and 20 were amended in the 1 May Paper. Claims 6, 13-17 and 19-25 are pending and under consideration.

Response to Amendment

Claim Rejections - 35 USC § 103

Rejection of claims 6, 13, 14, 17, 21, 24 and 25 under 35 U.S.C. 103(a) as being unpatentable over Baszczynski et al. US Patent No. 6,187,994 in view of Qin et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:1706-1710 is **withdrawn** in view of the amendment of claim 6 to recite that the recombinase encoded by the recombinase gene in the first nucleic acid molecule inverts a sequence in the second nucleic acid molecule.

Rejection of claims 15 and 16 under 35 U.S.C. 103(a) as being unpatentable over Baszczynski et al. (*supra*) in view of Qin et al. (*supra*) and further in view of Fitzmaurice et al. WO 93/07257 is **withdrawn** in view of the amendment of claim 6, from which the claims

depend, to recite that the recombinase encoded by the recombinase gene in the first nucleic acid molecule inverts a sequence in the second nucleic acid molecule.

Rejection of claims 6, 17 and 19-23 under 35 U.S.C. 103(a) as being unpatentable over Moller et al. US Patent No. 6,723,896 B1 is **withdrawn** in view of the amendment of claim 6 to recite that the recombinase encoded by the recombinase gene in the first nucleic acid molecule inverts a sequence in the second nucleic acid molecule and when the sequence inverted in the second nucleic acid molecule is said target gene, the expression of the target gene is inactivated.

New Grounds

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19 and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The MPEP states, "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. §112, first paragraph-written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." (MPEP §2163.06). The MPEP further states,

"Whenever the issue arises, the fundamental factual inquire is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed…If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in the application" (*Id.*, §2163.02). The introduction of claim changes which involve narrowing the claims by introducing elements or limitations which are not supported by the as-filed disclosure is a violation of the written description requirement of 35 U.S.C. 112, first paragraph. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996).

Claim 18 has been amended such that it is now directed to a method wherein signal sequences flank a positive regulatory element of the target gene such that expression of the recombinase encode by the recombinase gene in the first nucleic acid molecule results in inversion of the positive regulatory element, and inactivation of expression of the target gene.

Similarly, claim 20 has been amended such that it is now directed to a method wherein signal sequences flank a negative regulatory element of the target gene such that expression of the recombinase encode by the recombinase gene in the first nucleic acid molecule results in inversion of the positive regulatory element, and activation of expression of the target gene.

In contrast, the teachings of the originally filed disclosure directed to inversion of positive regulatory elements of the second nucleic acid molecule state that signal sequences flanking an inverted positive regulatory element of the target gene are configured so that

expression of the recombinase results in inversion of the inverted positive regulatory element and activation of expression of the target gene. (Page 7, lines 9-13.)

Likewise, the teachings of the originally filed disclosure directed to inversion of negative regulatory elements of the second nucleic acid molecule state that signal sequences flanking an inverted negative regulatory element of the target gene are configured so that expression of the recombinase results in inversion of the inverted positive regulatory element and inactivation of expression of the target gene. (Page 7, lines 13-17.)

These are the only teachings directed to inversion of regulatory elements in the second nucleic acid molecules and the effects of inversion (i.e., gene activation or inactivation) are directly opposite what is presently claimed in claims 19 and 20. Therefore, the subject matter claimed in amended claims 19 and 20 is not supported by the disclosure as originally filed and constitutes impermissible new matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, 13-17 and 19-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is indefinite in the recitation of "said target gene" in line 16 and "said target gene is inactivated" in line 18. The antecedent of "said target gene" could be "a target gene" of the preamble or "a target gene" of the second nucleic acid molecule recited in line 6 of the claim. As these two target genes are not necessarily the same, the antecedent of "said target gene" as

recited in the subsequent steps is unclear. If it is applicant's intention that the target gene modulated by the method (i.e., the target gene of the preamble) is the target gene comprised by the second nucleic acid molecule, it would be remedial to amend "a target gene" recited in line 6 to read "said target gene" such that it is clear that the target gene comprised by the second nucleic acid molecule is the target gene that is modulated in the method.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6, 15-17, and 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moller et al. US Patent No. 6,723,896 B1 (previously made of record) in view of Odell et al. US Patent No. 5,658,772.

The claims are directed to a method for modulating a target gene in a cell comprising introducing into the cell a first nucleic acid comprising a recombinase gene operably linked to an expression control sequence and signal sequences recognized by a recombinase encoded by the recombinase gene and a second nucleic acid molecule comprising a target gene and signal sequences recognized by the recombinase encoded by the first nucleic acid molecule. The method further requires that the recombinase encode by the recombinase gene in the first nucleic acid molecule, when expressed in the cell, excises a sequence in the first nucleic acid molecule located between the signal sequences, which excision results in modulation of expression of the recombinase gene. In addition, the method requires that the recombinase encoded by the recombinase gene in the first nucleic acid molecule, when expressed in the cell, inverts a sequence in said second nucleic acid molecule that is located between the signal sequences in the second nucleic acid molecule and the excision results in modulation of expression of the target gene, wherein when the sequence inverted in the second nucleic acid molecule is the target gene the expression of the target gene is inactivated. Finally, the claims require that the signal sequences for the first and second nucleic acid are not the same sequences.

It is particularly noted that the proviso that expression of the target gene is inactivated is in effect only "when the sequence inverted in the second nucleic acid molecule is said target gene". Therefore, the claim reads on a method wherein the sequence inverted in the second nucleic acid molecule is other than a target gene and expression of the target gene is activated.

Moller et al. teaches a method of modulating expression of a target gene in a plant cell comprising introducing a nucleic acid comprising a first nucleic acid sequence comprising a recombinase gene operably linked to an expression control sequence and a second nucleic acid

sequence comprising a target gene and signal sequences recognized by the recombinase of the first nucleic acid sequence. In one embodiment, the nucleic acid of Moller et al. is configured such that expression of the recombinase in the cell activates expression of the target gene by inverting the gene such that it is in the sense orientation with respect to the promoter sequence comprised by the second nucleic acid molecule. See especially Figure 3 (reproduced herein below), the caption thereto and the first full paragraph in column 6.

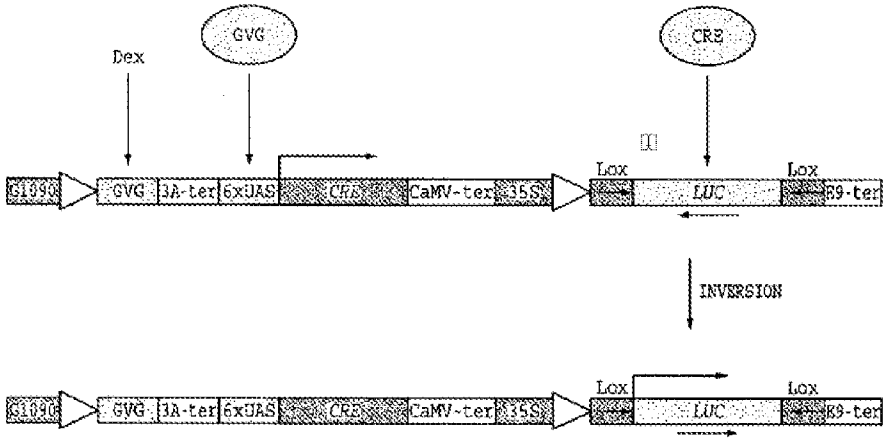

FIG. 3

Although Moller et al. teaches activation of the target gene by inversion of the target gene itself, it was known in the art at the time the invention was made that the same end (i.e., activation of a target gene) could be achieved by inverting a promoter or regulatory nucleotide sequence with respect to the target gene. For example, Odell et al. teaches,

> "[F]lipping, occurs when the lox sites are in reverse orientation on the same DNA molecule. This event may provide new methods of cre-regulated gene expression. Gene expression can be turned on by changing the direction of a promoter or regulatory nucleotide sequence from an inactive to an active orientation with respect to a coding region. Also changing the orientation of a coding region with respect to a promoter will alter its expression."

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute activation of the target gene by inversion of a regulatory nucleotide sequence for activation by inversion of the target gene in the second nucleotide sequence as taught in the method of Moller et al. In *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007), the Supreme Court particularly emphasized "the need for caution in granting a patent based on a combination of elements found in the prior art," (*Id.* At 1395) and discussed circumstances in which a patent might be determined to be obvious. Importantly, the Supreme Court reaffirmed principles based on it precedent that "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." (*Id.* At 1395.)

In the instant case, the method of Moller et al. differs from the method of the instant claims in that Moller et al. substitutes inversion of the target gene for inversion of a regulatory element to activate expression of the target gene. However, the teachings of Moller et al. demonstrate that inversion of regulatory sequences by Cre/Lox was recognized in the art as an alternative means of activating expression of target genes in plant cells. Therefore, one of skill in the art could have substituted inversion of a regulatory element for inversion of the target gene in the method of Moller et al. and the substitution would have predictably resulted in activated expression of the target gene. Thus, elements of the claimed method were known to one of ordinary skill in the art at the time the invention was made, one could have substituted one known element for another element known in the art and the substitution would have yielded nothing more than predictable results to one of ordinary skill in the art at the time of invention. Therefore, practicing the method wherein activation of the target gene is achieved by inversion

of a regulatory element in the second nucleic acid molecule would have been obvious to one of ordinary skill in the art at the time the invention was made.

The method of Moller et al. in view of Odell et al. comprises all of the elements of the method presently claimed except that Moller et al. does not explicitly teach the inclusion of signal sequences recognized by the recombinase in the first nucleic acid molecule such that the expression of the recombinase excises a sequence from the first nucleic acid molecule resulting in modulation of expression of the recombinase gene.

However, Moller et al. further teaches a method "to excise and remove transgenes (e.g., antibiotic resistance markers) from transgenic plants once used and no longer needed. "These 'suicide' gene cassettes, including the recombination system itself, can therefore be evicted from the plant genome once their function has been exerted." (Column 2, lines 54-59; emphasis added herein.) This system is illustrated in Figures 4-5, which are reproduced herein below.

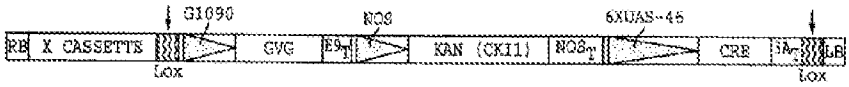

FIG. 4

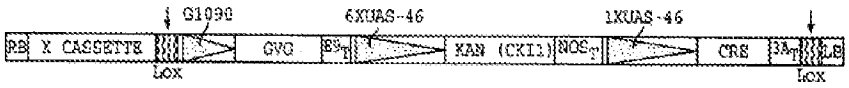

FIG. 5

Note that Moller et al. teaches that the suicide gene cassette comprising the recombinase is included with an "X CASSETTE", which is identified in the caption as a transgene encoding a genetic trait of interest.

It would have been obvious to one of ordinary skill in the art to modify the nucleic acid illustrated in Figure 1 of Moller et al. by the substitution of a suicide cassette comprising a recombinase gene flanked by lox sites such that expression of the recombinase results in excision and inactivation of the recombination system as taught in Figures 4-5 and column 2 of Moller et al. One would be motivated to do so in order to obtain the expected benefit of marker gene expression and recombinase activity provided by the suicide cassette and because Moller et al. teaches "The ability to specifically remove transgenes from transgenic plants offers a way of engineering desired genetic traits into crop species without the presence of potentially environmentally unfriendly transgenes such as antibiotic resistance markers." (First paragraph in column 5.) Absent evidence to the contrary, one would have a reasonable expectation of success in combining the elements of the prior art because Moller et al. demonstrates the operability of each system and there is no reason to expect that the elements would not operate together.

In view of the foregoing, the invention of independent claim 6, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made.

Furthermore, the elements of the dependent claims are also found in the teachings of Moller et al. and Odell et al. Specifically, Odell et al. teaches that methods using Cre/lox regulation of gene expression can be used to produce seedless fruit by tissue specific expression of Cre recombinase. (See especially the section bridging columns 13-14, in particular column 14, lines 18-20.) These teachings of Odell et al. render obvious the method of claims 15 and 16. The signal sequences in the second nucleic acid molecule are in inverted orientation with one another according to the instant claim 17 (see especially Figure 1); the signal sequences in the first nucleic acid flank both the recombinase gene and positive regulatory elements in the

recombinase gene according to the instant claims 21 and 22; the first and second nucleic acid molecules in the construct of Moller et al. are present in the same vector according to the instant claim 23; Odell et al. teaches that the nucleic acid comprising the recombinase and the nucleic acid encoding the target gene can be present on separate vectors according to claim 24; and both Moller et al. and Odell et al. teach the Cre/lox system according to claim 25.

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Moller et al. in view of Odell et al., as applied to claim 6 herein above, and further in view of Baszczynski et al. US Patent No. 6,187,994 (previously made of record).

Claim 13 is directed to the method of claim 6, wherein the target gene encodes a disease resistance protein. As described above, the method of claim 6, as a whole, would have been obvious to one of ordinary skill in view of the teachings of Moller et al. in view of Odell et al. Moller et al. and Odell et al. do not specify that the target gene might encode a disease resistance protein. However, Moller et al. teaches that the system described therein is generally useful for activating transgenes in plants. Baszczynski et al. teaches that it was known in the art at the time of invention that Cre/lox systems for obtaining gene expression could be used to express genes effecting plant susceptibility to disease (i.e., disease resistance genes; see especially the second full paragraph in column 7).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include disease resistance genes among those expressed by the method of Moller et al. in view of Odell et al. One would be motivated to do so in order to obtain the expected benefit of disease resistance in the plant of interest. Absent evidence to the contrary, one would have a

reasonable expectation of success in expressing a disease resistance gene by the method of Moller et al. in view of Odell et al. because the method is generally useful for expressing any gene and Baszczynski et al. teaches that genes effecting disease susceptibility could be expressed in plants.

In view of the foregoing, the claimed invention as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the claims are properly rejected under 35 USC § 103(a) as obvious over the art.

Response to Arguments

Applicant's arguments regarding previous rejection of the claims as obvious over Moller et al. are addressed herein to the extent that they are relevant to the new rejection of the claims as obvious over Moller et al. in view of Odell et al. Applicant first contends that Moller et al. does not teach a critical element of the instant invention--the self-extinguishing recombinase feature of the instant claims. Applicant submits that the constructs of Figure 1 as taught by Moller do not comprise a recombinase gene flanked by signal sequences and, hence, expression of the recombinase does not lead to inactivation of the recombinase as required by the claimed invention. While acknowledging that Moller further describes a second series of constructs which modulate transgenes, e.g. sequences that are incorporated into the plant genome, called suicide cassettes (Figures 4 and 5), describes methods of excising inserted silent transgenes, or stuffer fragments, from the genomic sequence in order to activate genes, and teaches methods of activating genes by inverting transgenes that had previously been inserted into the genome in an

antisense orientation, Applicant submits that Moller et al. fails to teach inactivation of genes by inversion of sequences.

These arguments are not persuasive, as described in the *prima facie* rejection, Moller et al. teaches a method to excise and remove transgenes from transgenic plants once used and no longer needed. Moller et al. teaches that these "suicide" gene cassettes, including the recombination system itself, can therefore be evicted from the plant genome once their function has been exerted. Moller et al. illustrates this suicide cassette configuration wherein the entire Cre recombinase gene is flanked by lox sites. As Moller et al. teaches that the genes comprised within the suicide cassette are removed once they are no longer needed (i.e., inactivated), the suicide cassette illustrated in Figures 4 and 5 clearly comprises a self excising and self extinguishing Cre recombinase. With regard to inactivation of genes by inversion of sequences, it is noted that the claims only require inactivation "when the sequence inverted in said second nucleic acid molecule is said target gene". As described above, the claims are obvious over the art, at least, because it would have been obvious to modify the method of Moller et al. to activate the transgene by a method wherein a regulatory sequence of the second nucleic acid molecule is inverted. As this embodiment is within the scope of the instant claims, the claimed invention would have been obvious to one of skill in the art at the time the invention was made.

Applicant submits that because Moller et al. does not explicitly teach the inclusion of signal sequences recognized by the recombinase in the first nucleic acid molecule such that the expression of the recombinase excises a sequence from the first nucleic acid molecule resulting in modulation of expression of the recombinase gene Moller et al. necessarily fails to teach, suggest, or demonstrate that signal sequences for the first nucleic acid and the second nucleic

acid are not the same sequences. According to Applicant, the claimed invention further requires that signal sequences for the first nucleic acid and the second nucleic acid are not the same sequences while the constructs of Moller do not employ more than one type of signal sequence.

This argument is not persuasive, it is first noted that the claims do not require that the signal sequences of the first and second nucleic acid are different "types". In fact, the claims require that the signal sequences in the first and second nucleic acid molecules are a substrate for the same recombinase. Therefore, the broadest reasonable reading of the claims requires only that the signal sites of the first and second nucleic acid molecule are not one and the same (i.e., do not occupy the same space on the nucleic acid molecules). This configuration would have been obvious in view of the teachings of Moller et al. because Moller et al. teaches that the signal sites of the suicide cassette operate to remove the cassette from the plant while the signal sites of the nucleic acid encoding the target gene activate expression. The only way that both of those outcomes could be achieved is if the signal sequences of the first and second nucleic acid molecules are different.

Applicant submits that the claimed methods teach introducing active genes and a recombinase into plant cells which provide a therapeutic gene product for a desired amount of time until the provided recombinase shuts down expression of the active target gene and the recombinase itself and contends that Moller et al. fails to teach methods of gene inactivation using gene inversion. Applicant further contends that Moller et al. fails to combine gene inactivation, gene inversion, and a self-excising recombinase in the same construct and does not teach or suggest a method of gene inactivation in which a target gene is irreversibly inverted by a

self-excising recombinase. Applicant further submits that Moller et al. teaches away from inactivating transgenes by a method involving inversion of the transgene.

These arguments are not persuasive. As pointed out herein above, the claims do not require gene inactivation. Therefore, even if one accepts that the art does not render obvious gene inactivation by inversion, *arguendo*, for the reasons stated in the *prima facie* rejection the art still renders obvious what is presently claimed.

Finally, Applicant submits that there is no objective reason provided in Moller et al. that would lead the skilled artisan to arrive at the claimed invention. Moreover, according to Applicant, there is no evidence that the results of combining the elements of the Moller constructs would have been predictable, particularly in light of the inability of Moller himself, to identify and successfully use these elements to inactivate a gene. Thus, applicant asserts that any suggestion that it would have been obvious that the inclusion of lox sites flanking the recombinase gene would result in excision of the recombinase and inversion of the target sequence is an improper application of hindsight based on Applicant's disclosure in the instant application.

These arguments are also not persuasive. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, all of the

knowledge relied upon in making the instant invention was available in the art at the time of invention and, for the reasons stated above, combining the elements as required by the claims would have been obvious to one of ordinary skill in the art at the time the invention was made given that inversion of a target gene and inversion of a regulatory element such that it is operably linked to a target gene were recognized in the art as alternative means of achieving gene activation. With regard to whether one would reasonably expect to be able to use the prior art elements to inactivate a gene, the point is moot because the claims do not require that the gene is inactivated when a regulatory element in the second nucleic acid molecule is inverted.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand properly rejected under 35 USC § 103(a) as obvious over the art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M. Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D. can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel M Sullivan/
Primary Examiner
Art Unit 1636